

# **New Strategies for Regulatory Approval of In Vitro Technologies for Drug Development**

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# **How are new technologies accepted today in regulatory agencies?**

- **Accepted over time**
- **Drug-dependent context of use**
  - **Original Submission**
  - **Labeling Updates**
  - **Codevelopment of drug and test**
- **Drug-independent context of use**
  - **Qualification Process for Drug Development Tools**

# Qualification

- **Goal is to make sure that information in regulatory submissions is acceptable to regulatory agencies.**
- **The concept of qualification in this case is circumscribed to the requirements of regulatory review.**
- **Not all new technologies need to be qualified, and not all new technologies may be qualified through a drug development tool qualification regulatory process.**

# Guidance for Industry

## Qualification Process for Drug Development Tools

### ***DRAFT GUIDANCE***

**This guidance document is being distributed for comment purposes only.**

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Shaniece Gathers, 301-796-2600.

U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research (CDER)

October 2010  
Clinical/Medical

# Qualification in the Guidance

- ***Definition:*** A conclusion that within the stated *context of use*, the results of assessment can be relied upon to have a specific interpretation and application in drug development and regulatory decision-making.
- ***Regulatory implication:*** If a drug development tool is qualified,
  - Analytically valid measurements of it can be relied upon to have a specific use and interpretable meaning in drug development.
  - The qualification process is expected to expedite development of successful marketing applications.
  - If qualified for a specific context of use,
    - industry can use the drug development tool for the qualified purpose during drug development
    - CDER reviewers can be confident in applying the DDT for the qualified use without the need to reconfirm the DDT's utility.

# Context of Use

- **Comprehensive statement that:**
  - **fully and clearly describes the manner and purpose of use for the drug development tool**
  - **all important criteria regarding the circumstances under which the drug development tool is qualified**
  - **defines the boundaries within which the available data adequately justify use**
  - **potential value outside these boundaries**
    - **data from additional studies obtained over time may be submitted to expand the qualified context of use**

# Context of Use

- **Drug Efficacy Assessment Definition for Qualification**

- *A conclusion that within the context of use of target identification and characterization, the results of the tests can be relied upon to have a specific interpretation and application in drug development.*
- **Does this context of use require regulatory qualification?**
  - Only if the test is to be used to make clinical decisions about a patient.
  - No explicit regulatory qualification is needed if the test is only used during early or intermediate steps in drug development.

- **Drug Safety Assessment Definition for Qualification**

- *A conclusion that within the context of use of drug safety assessment at a molecular level, the results of the tests can be relied upon to have a specific interpretation and application in drug development.*
- **Does this context of use require regulatory qualification?**
  - Yes, because the application of these tests in non clinical safety assessment regulatory review requires qualification.
    - Previous to Phase 1
    - During and after Phase 1

# **Drug Efficacy Assessment Definition for Qualification**

- **Internal decision-making within a drug company.**
  - **No regulatory qualification needed.**
- **Result triggers a drug-specific clinical decision for a patient.**
  - **Scenario 1**
    - **Companion diagnostic**
  - **Scenario 2**
    - **Clinical trial enrichment**



# **Drug Safety Assessment**

## **Definition for Qualification**

- **Internal decision-making within a drug company.**
  - No regulatory qualification needed.
- **Regulatory Submissions: *must redefine drug safety assessment along molecular mechanisms of toxicity***
  - **Drug-dependent safety assessment**
    - Very unlikely application leading to regulatory submission.
  - **Drug-independent qualification**
    - Consortium to show data supporting correlation between in vitro test and ranking in humans for drug models tested.

# **Redefinition of drug safety assessment along molecular mechanisms of toxicity**

- **Models and tests developed can measure specific molecular parameters associated with toxicity.**
- **These models do not necessarily measure pathological outcomes identical to those measured in animal models or in humans.**
- **Specific molecular parameters associated with toxicity may be correlated with rankings for the toxicity in humans for model drugs.**

# **Summary of Recommendations for Qualification of In Vitro Tests**

- **Efficacy applications**
  - **Internal decision-making: none**
  - **Companion diagnostic: CDRH approval**
  - **Clinical study enrichment with no diagnostic application: none**
- **Safety applications**
  - **Internal decision-making: none**
  - **Nonclinical and clinical drug safety applications: qualification against a molecular pathways and mechanisms of toxicity measured in the in vitro system.**

# Qualification Process at CDER



[http://c-path.org/PROSlides/Workshop3/2012\\_PROConsortium\\_FDA\\_DDT\\_Qualification.pdf](http://c-path.org/PROSlides/Workshop3/2012_PROConsortium_FDA_DDT_Qualification.pdf)

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284621.htm>